GNAQ gene

G protein subunit alpha q

Normal Function

The *GNAQ* gene provides instructions for making a protein called guanine nucleotide-binding protein G(q) subunit alpha (Gαq). The Gαq protein is part of a group of proteins called the trimeric G protein complex. This complex attaches (binds) to other proteins called G protein coupled receptors. When the protein complex is bound to a receptor, the Gαq protein binds to a molecule called GTP and is turned on (activated). The activated Gαq protein then separates from the protein complex and activates signaling pathways that help to regulate the development and function of blood vessels. The Gαq protein converts GTP to a similar molecule called GDP, which turns off (inactivates) the protein. It then reattaches to the trimeric G protein complex, turning off the signaling pathways.

Health Conditions Related to Genetic Changes

Sturge-Weber syndrome

At least one mutation in the *GNAQ* gene has been found to cause Sturge-Weber syndrome. Sturge-Weber syndrome is a condition that affects the development of certain blood vessels and often leads to three major features: a red or pink birthmark called a port-wine birthmark, brain abnormalities, and increased pressure in the eye (glaucoma) or other eye problems. The *GNAQ* gene mutation associated with Sturge-Weber syndrome changes a single building block (amino acid) in the Gαq protein. It replaces the amino acid arginine with the amino acid glutamine at position 183 in the Gαq protein (written as Arg183Gln or R183Q). This mutation is not inherited but occurs after conception. This alteration is called a somatic mutation and is present only in certain cells, specifically cells in the brain, eyes, and skin that are involved in blood vessel formation.

Following its activation, the altered Gαq protein cannot convert GTP to GDP. As a result, the protein is always active, and signaling pathways controlled by it are constantly turned on. This increased signaling likely disrupts the regulation of blood vessel development, causing abnormal and excessive formation of vessels before birth in people with Sturge-Weber syndrome.

other disorders

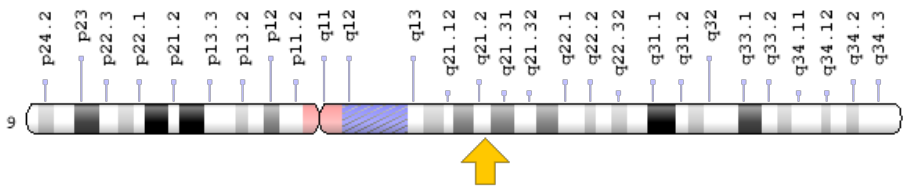
The R183Q mutation in the *GNAQ* gene can also cause port-wine birthmarks without the brain or eye abnormalities that are often associated with Sturge-Weber syndrome (described above). As in Sturge-Weber syndrome, isolated port-wine birthmarks caused by a *GNAQ* gene mutation are usually on one side of the face but can be on both sides. It is thought that somatic *GNAQ* gene mutations that cause isolated port-wine birthmarks occur later in fetal development than those that cause Sturge-Weber syndrome and so affect fewer cells and tissues.

Somatic mutations in the *GNAQ* gene have also been found in an eye cancer called uveal melanoma. This cancer occurs in the middle layer of the eye called the uvea. The uvea includes the colored portion of the eye (the iris) and related tissues that underlie the white part of the eye (the sclera). The *GNAQ* gene mutations in uveal melanoma result in an overactive protein, which leads to excessive signaling. This abnormal signaling likely contributes to the overgrowth of cells and to the formation of a cancerous tumor. While the R183Q mutation has been found in uveal melanoma, individuals with Sturge-Weber syndrome or isolated port-wine birthmark do not have an increased risk of this form of cancer. *GNAQ* gene mutations that lead to uveal melanoma usually occur later in a person's life, typically in adulthood, and are limited to the cells that give rise to the tumor.

Chromosomal Location

Cytogenetic Location: 9q21.2, which is the long (q) arm of chromosome 9 at position 21.2

Molecular Location: base pairs 77,716,274 to 78,031,449 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- G-ALPHA-q
- GAQ
- guanine nucleotide binding protein (G protein), q polypeptide

- guanine nucleotide-binding protein alpha-q
- guanine nucleotide-binding protein G(q) subunit alpha

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): The Functional Activity of G Proteins Involves Their Dissociation and Reassociation in Response to Extracellular Signals
  https://www.ncbi.nlm.nih.gov/books/NBK28116/#A1411
- Biochemistry (fifth edition, 2002): G Proteins Cycle Between GDP- and GTP-Bound Forms
  https://www.ncbi.nlm.nih.gov/books/NBK22592/#A2060
- Molecular Biology of the Cell (fourth edition, 2002): Trimeric G Proteins Disassemble to Relay Signals from G-Protein-linked Receptors
  https://www.ncbi.nlm.nih.gov/books/NBK26912/#A2796
- National Cancer Institute: Intraocular (Uveal) Melanoma Treatment PDQ
  https://www.cancer.gov/types/eye/patient/intraocular-melanoma-treatment-pdq#section/_1

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GNAQ%5BTIAB%5D%29+OR+%28G+protein+subunit+alpha+q%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D

OMIM

- CAPILLARY MALFORMATIONS, CONGENITAL
  http://omim.org/entry/163000
- GUANINE NUCLEOTIDE-BINDING PROTEIN, Q POLYPEPTIDE
  http://omim.org/entry/600998
- MELANOMA, UVEAL
  http://omim.org/entry/155720

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GNAQID43280ch9q21.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GNAQ%5Bgene%5D

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4390
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/2776
- UniProt
  http://www.uniprot.org/uniprot/P50148

Sources for This Summary

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26564078
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  http://omim.org/entry/600998
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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23656586
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